

# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP2004/006943

**A. CLASSIFICATION OF SUBJECT MATTER**  
IPC 7 C07K14/815 A61K38/58

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, WPI Data, PAJ

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 028 170 A (KU ET AL) 22 February 2000 (2000-02-22) "Analog of hirudin" abstract column 2, line 13 - line 67 ----- -/--	1-8

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

\* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*G\* document member of the same patent family

Date of the actual completion of the international search

4 July 2005

Date of mailing of the international search report

11 08. 2005

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>MURAMATSU RYO ET AL: "Existence of beta-methylnorleucine in recombinant hirudin produced by Escherichia coli." JOURNAL OF BIOTECHNOLOGY. 14 FEB 2002, vol. 93, no. 2, 14 February 2002 (2002-02-14), pages 131-142, XP002334171 ISSN: 0168-1656 abstract page 135, left-hand column, last paragraph - right-hand column, paragraph 1 page 140, right-hand column, last paragraph</p>	1-8
A	<p>BRAUN P J ET AL: "Use of site-directed mutagenesis to investigate the basis for the specificity of hirudin." BIOCHEMISTRY. 23 AUG 1988, vol. 27, no. 17, 23 August 1988 (1988-08-23), pages 6517-6522, XP002325668 ISSN: 0006-2960 abstract figure 1 table 1</p>	1-8
A	<p>DODT J ET AL: "Interaction of site specific hirudin variants with alpha-thrombin." FEBS LETTERS. 29 FEB 1988, vol. 229, no. 1, 29 February 1988 (1988-02-29), pages 87-90, XP001206241 ISSN: 0014-5793 abstract page 88, left-hand column, last paragraph - right-hand column, paragraph 1 table 1</p>	1-8
A	<p>KRSTENANSKY J L ET AL: "ANTICOAGULANT PEPTIDES NATURE OF THE INTERACTION OF THE CARBOXYL-TERMINAL REGION OF HIRUDIN WITH NONCATALYTIC BINDING SITE ON THROMBIN" JOURNAL OF MEDICINAL CHEMISTRY, vol. 30, no. 9, 1987, pages 1688-1691, XP002325669 ISSN: 0022-2623 abstract table III</p>	1-8

## INTERNATIONAL SEARCH REPORT

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### Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

### Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  
1, 2, 7, 8 in part and 3-6 completely
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

#### Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: claims 1-8 (partially)

A modified hirudin molecule having a substitution L → T at position 13 and a pharmaceutical composition comprising said molecule.

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Inventions 2-6: claims 1-8 (partially)

Modified hirudin molecules having a substitution L → T, A, H, Q or T at position 15 and a pharmaceutical composition comprising such a molecule.

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Inventions 7-14: claims 1-8 (partially)

Modified hirudin molecules having a substitution V → A, G, H, K, N, P, Q or R at position 21 and a pharmaceutical composition comprising such a molecule.

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Inventions (further): claims 1-8 (in part)

Modified hirudin molecules having a substitution at position 29, 30, 40, 47, 48, 53, or 57 and a pharmaceutical composition comprising said molecule.

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Inventions (further): claims 1-8 (in part)

All combinations of modifications at more than one position as referred to in claim 1 and a pharmaceutical composition comprising such a molecule.

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Inventions (further): claims 9 and 10

A peptide molecule as mentioned in claim 9 and its use for the manufacture of a modified hirudin molecule.

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP2004/006943

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6028170	A	22-02-2000	US 5837808 A	17-11-1998
			AU 7721594 A	27-03-1995
			WO 9507295 A1	16-03-1995
			WO 9304082 A1	04-03-1993
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